L11 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN
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DOCUMENT NUMBER: 144:51831
TITLE: Synthesis of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels
INVENTOR(S): Brummerhop, Harm; Frick, Wendelin; Glombik, Heiner; Plettenburg, Oliver; Bickel, Martin; Heuer, Hubert; Theis, Stefan
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
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CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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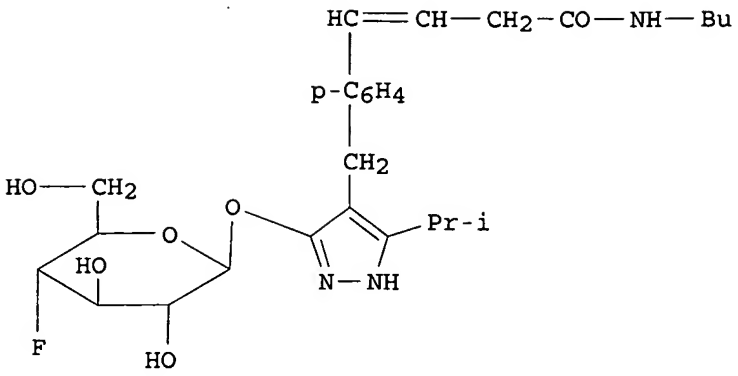
WO 2005121161	A1	20051222	WO 2005-EP5959	20050603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004028241	A1	20060105	DE 2004-102004028241	20040611
DE 102004028241	B4	20070913		
AU 2005252329	A1	20051222	AU 2005-252329	20050603
CA 2570042	A1	20051222	CA 2005-2570042	20050603
EP 1758914	A1	20070307	EP 2005-746637	20050603
EP 1758914	B1	20071121		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1964984	A	20070516	CN 2005-80019067	20050603
BR 2005010770	A	20071120	BR 2005-10770	20050603
US 2007197623	A1	20070823	US 2006-567410	20061206
KR 2007023726	A	20070228	KR 2006-726083	20061211
IN 2006CN04531	A	20070629	IN 2006-CN4531	20061211
NO 2007000176	A	20070309	NO 2007-176	20070110
PRIORITY APPLN. INFO.:			DE 2004-102004028241A	20040611
			WO 2005-EP5959 W	20050603

OTHER SOURCE(S): MARPAT 144:51831
GI



I

AB The invention relates to substituted fluoro-glycoside derivs. of pyrazoles, e.g. (I), and their physiol. compatible salts, which inhibit Na+-dependent glucose transporter 1 (SGLT-1) and to a method for their production Thus, 1-bromo-4-deoxy-4-fluoro-2,3,6-tri-O-benzoyl-α-D-glucopyranose was prepared from Me 2,3,6-tri-O-benzoyl α-D-galactopyranose in 3 steps, and reacted with 4-(4-bromo-benzyl)-5-isopropylpyraz-3-ol, prepared from Me 4-methyl-3-oxopentanoate in 2 steps, to give the β-linked pyrazole intermediate (II). II was then reacted with 3-butenoic acid, followed by a condensation reaction with n-butylamine and deprotection of the sugar oxygens to give I. In in vitro tests using CHO-TRex-hSGLT1 cell line (derivation given), measuring the concentration at which uptake of Me α-D-glucopyranoside was reduced by 50%, I had IC50 value of 0.043 μM.

IT 871484-07-0P 871484-13-8P 871484-14-9P
871484-15-0P 871484-16-1P 871484-17-2P
871484-18-3P 871484-19-4P 871484-20-7P
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871484-27-4P 871484-28-5P 871484-29-6P
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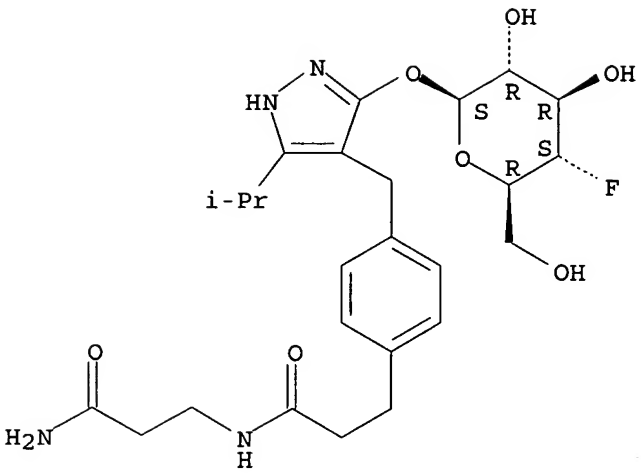
871484-45-6P 871484-46-7P 871484-47-8P
871484-48-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

RN 871484-07-0 HCAPLUS

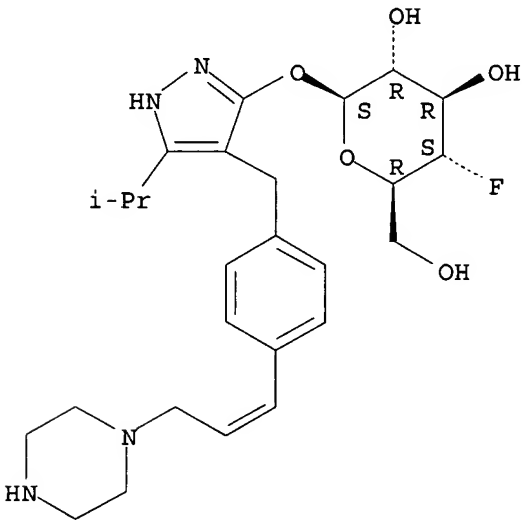
CN Benzenepropanamide, N-(3-amino-3-oxopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



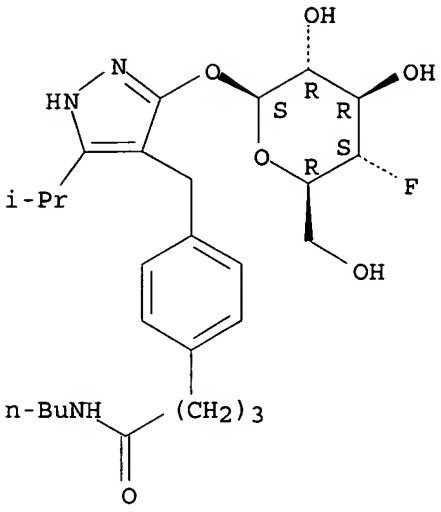
RN 871484-13-8 HCAPLUS
CN β-D-Glucopyranoside, 5-(1-methylethyl)-4-[[4-[3-(1-piperazinyl)-1-propenyl]phenyl]methyl]-1H-pyrazol-3-yl 4-deoxy-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



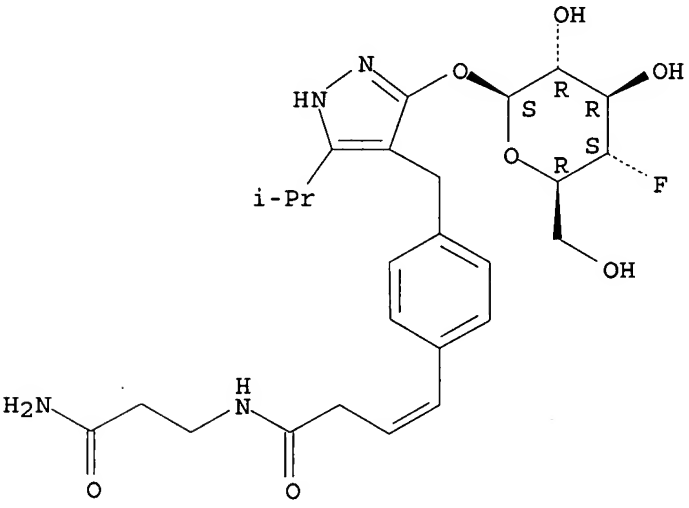
RN 871484-14-9 HCAPLUS
CN Benzenebutanamide, N-butyl-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



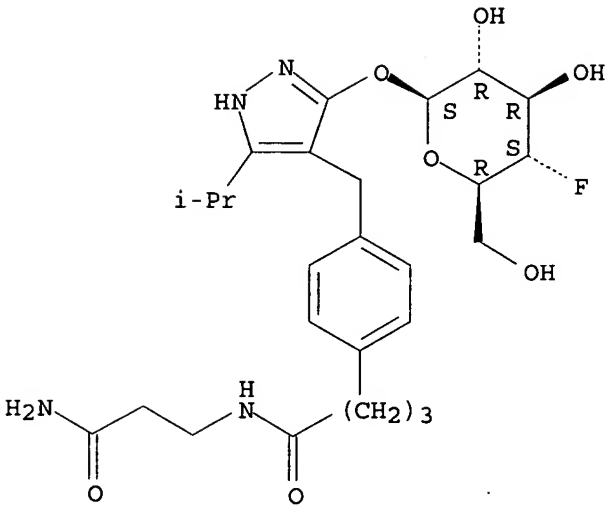
RN 871484-15-0 HCAPLUS
CN 3-Butenamide, N-(3-amino-3-oxopropyl)-4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



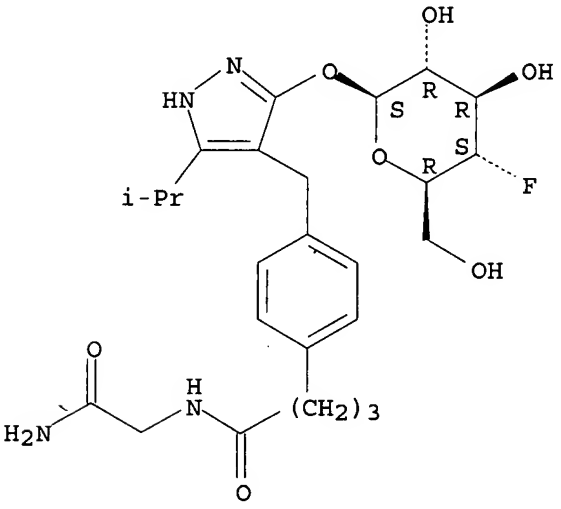
RN 871484-16-1 HCAPLUS
CN Benzenebutanamide, N-(3-amino-3-oxopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



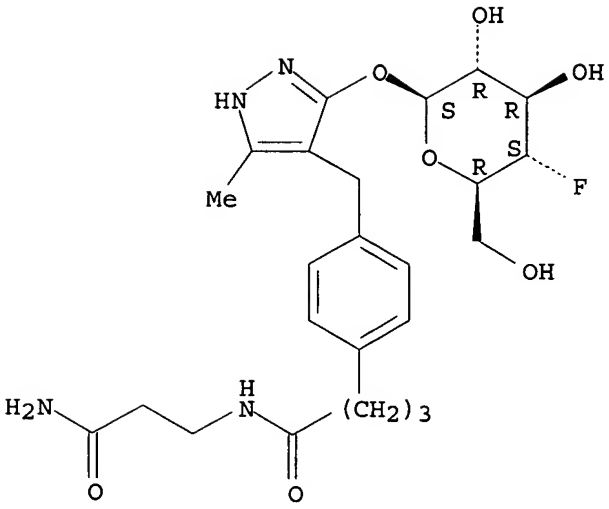
RN 871484-17-2 HCAPLUS
CN Benzenebutanamide, N-(2-amino-2-oxoethyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



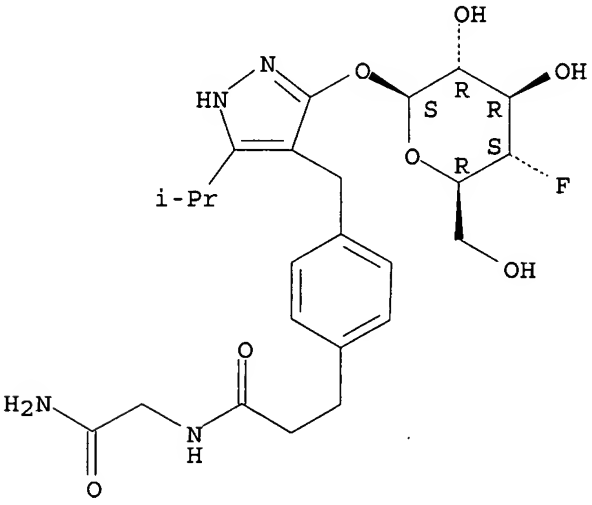
RN 871484-18-3 HCAPLUS
CN Benzenebutanamide, N-(3-amino-3-oxopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-methyl-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



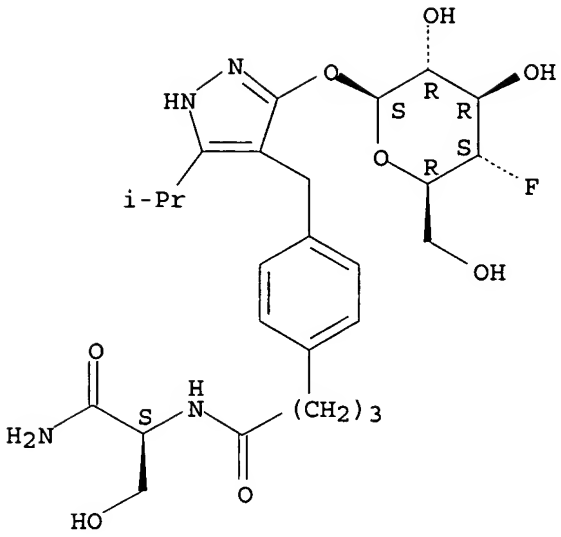
RN 871484-19-4 HCAPLUS
CN Benzenepropanamide, N-(2-amino-2-oxoethyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



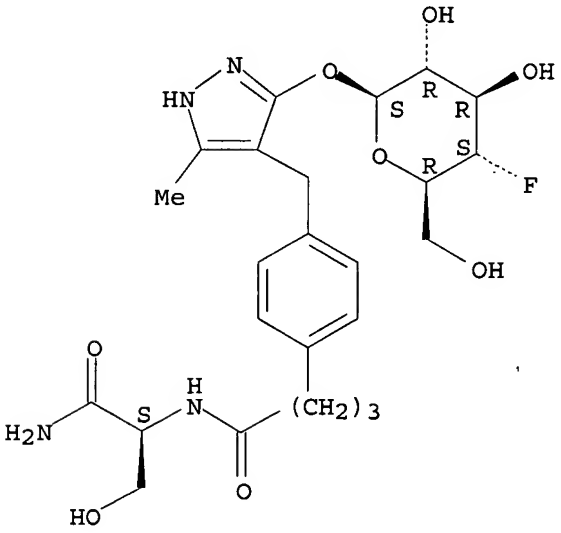
RN 871484-20-7 HCAPLUS
CN Benzenebutanamide, N-[(1S)-2-amino-1-(hydroxymethyl)-2-oxoethyl]-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



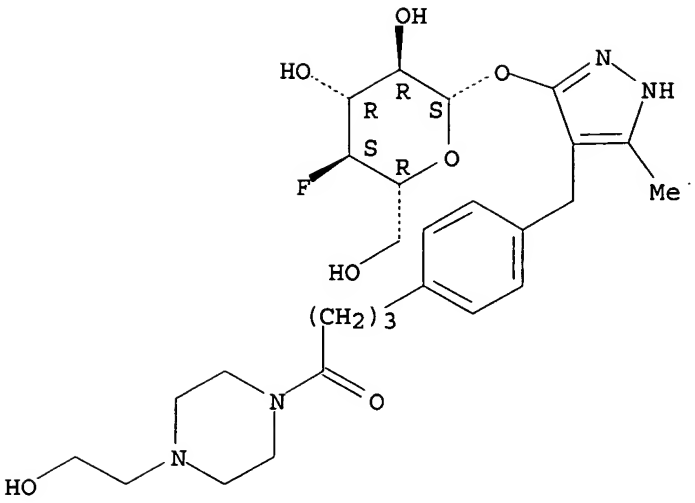
RN 871484-21-8 HCAPLUS
CN Benzenebutanamide, N-[(1S)-2-amino-1-(hydroxymethyl)-2-oxoethyl]-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-methyl-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



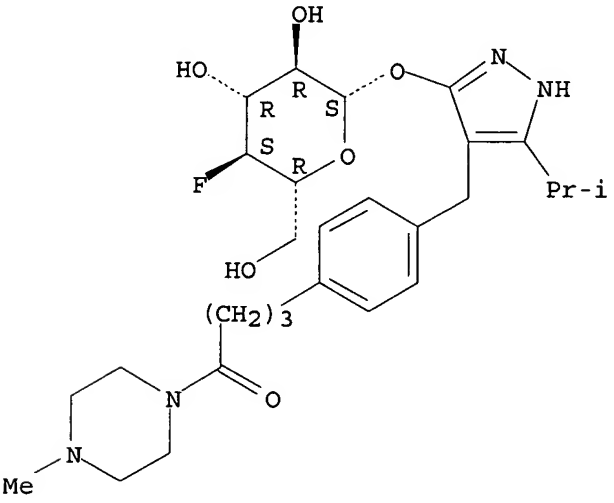
RN 871484-22-9 HCAPLUS
CN Piperazine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-methyl-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



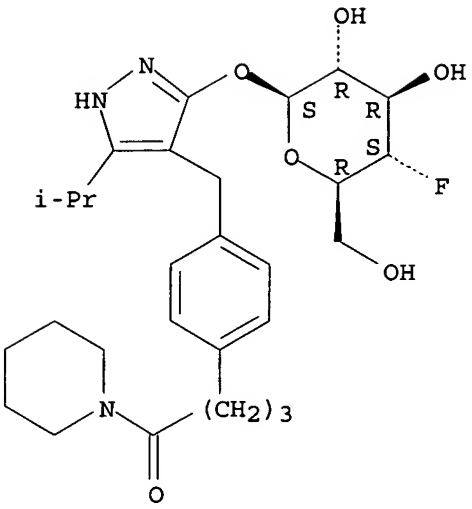
RN 871484-23-0 HCAPLUS
CN Piperazine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



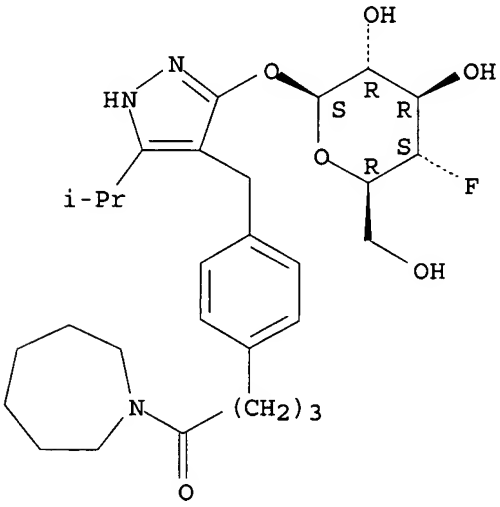
RN 871484-24-1 HCAPLUS
CN Piperidine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



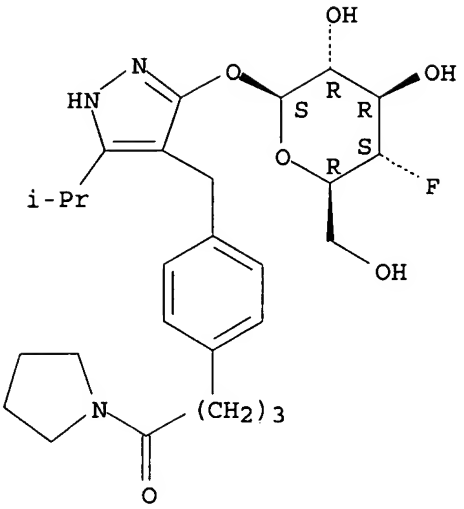
RN 871484-25-2 HCAPLUS
CN 1H-Azepine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



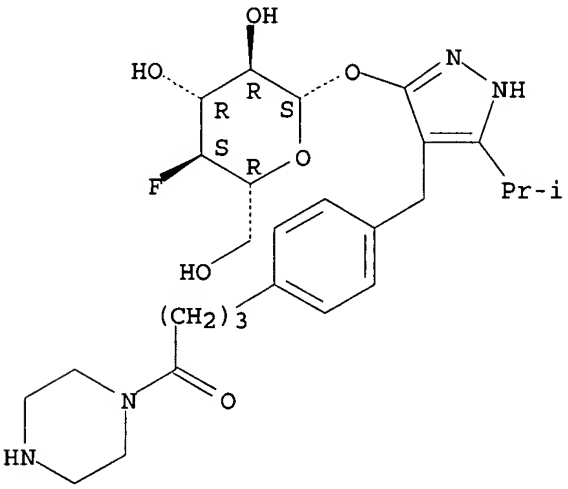
RN 871484-26-3 HCAPLUS
CN Pyrrolidine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



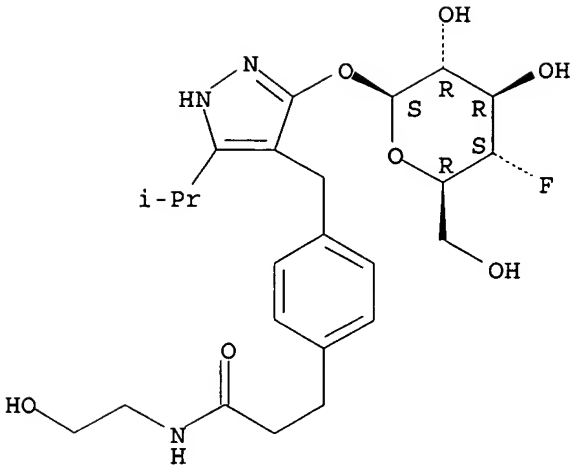
RN 871484-27-4 HCAPLUS
CN Piperazine, 1-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



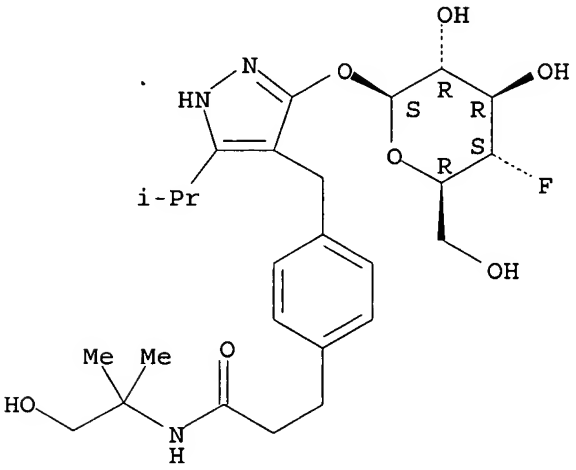
RN 871484-28-5 HCAPLUS
CN Benzenepropanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-(2-hydroxyethyl)- (CA INDEX NAME)

Absolute stereochemistry.



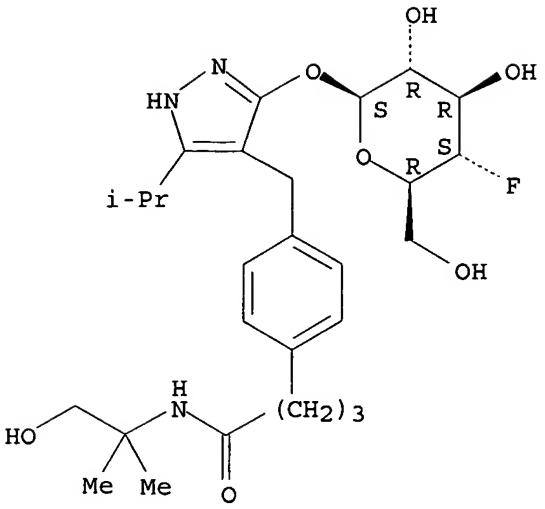
RN 871484-29-6 HCAPLUS
CN Benzenepropanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-(2-hydroxy-1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



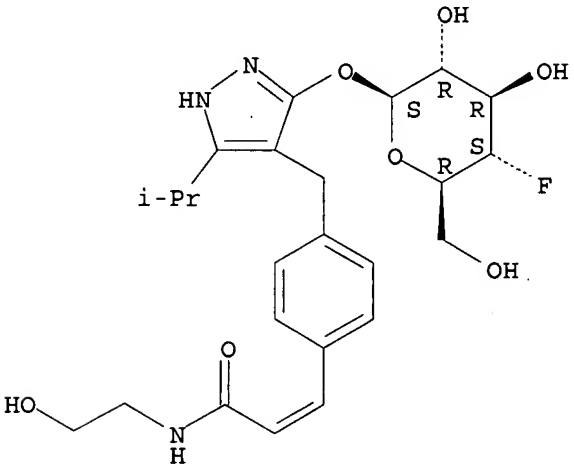
RN 871484-30-9 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-(2-hydroxy-1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



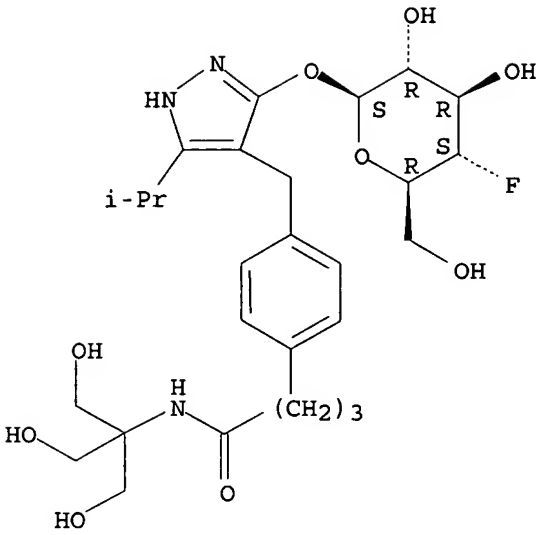
RN 871484-31-0 HCAPLUS
CN 2-Propenamide, 3-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-N-(2-hydroxyethyl)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



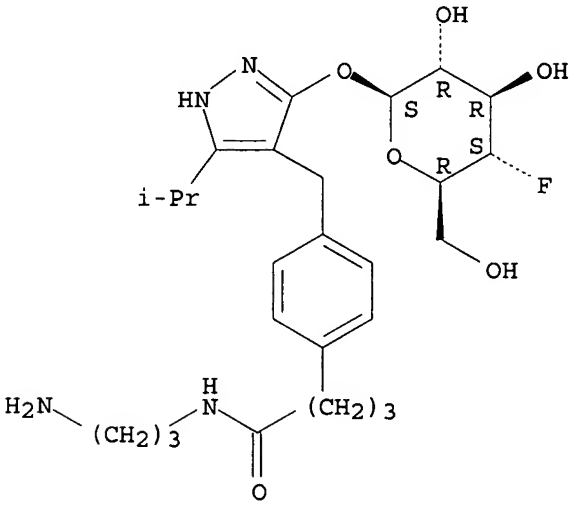
RN 871484-32-1 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



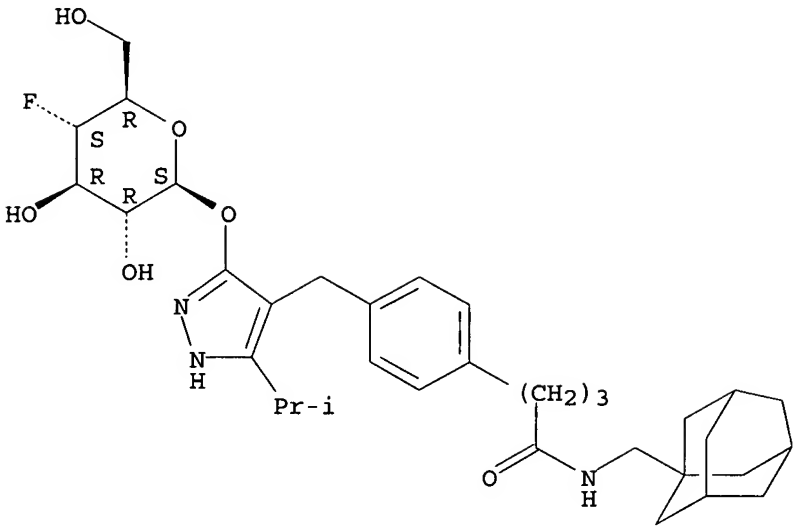
RN 871484-33-2 HCAPLUS
CN Benzenebutanamide, N-(3-aminopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



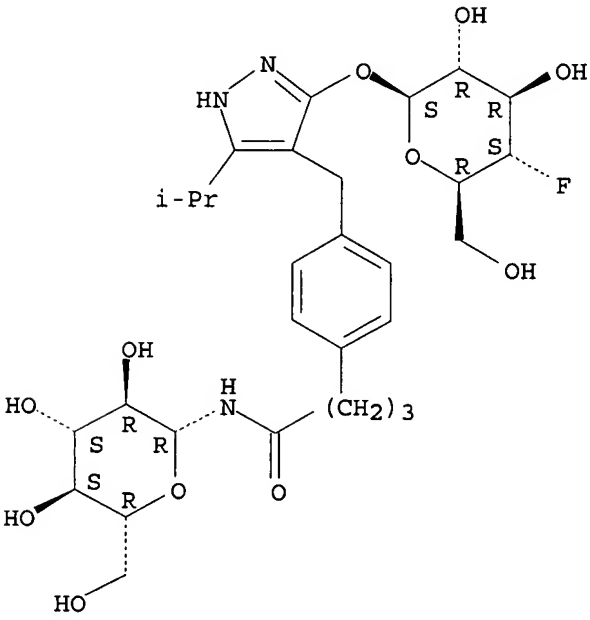
RN 871484-34-3 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-(tricyclo[3.3.1.13,7]dec-1-ylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



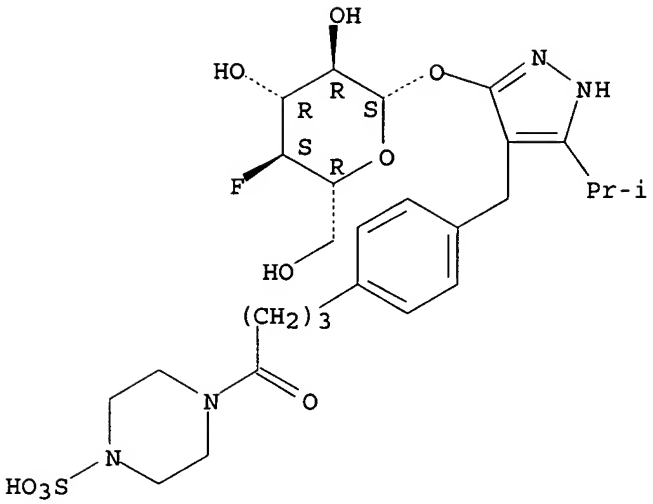
RN 871484-35-4 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-β-D-glucopyranosyl- (CA INDEX NAME)

Absolute stereochemistry.



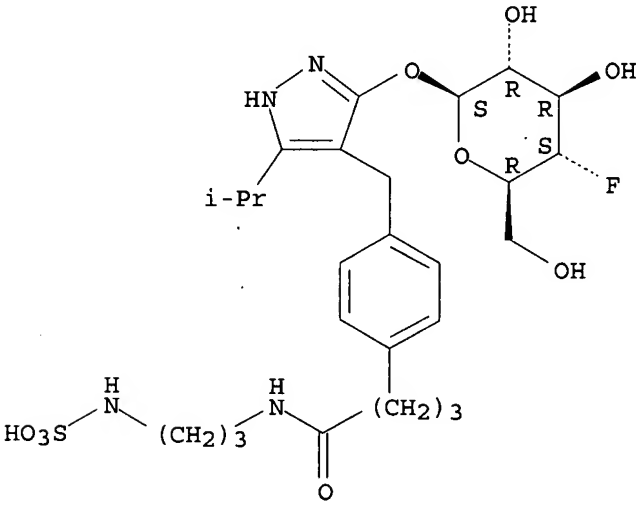
RN 871484-36-5 HCAPLUS
CN 1-Piperazinesulfonic acid, 4-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]- (CA INDEX NAME)

Absolute stereochemistry.



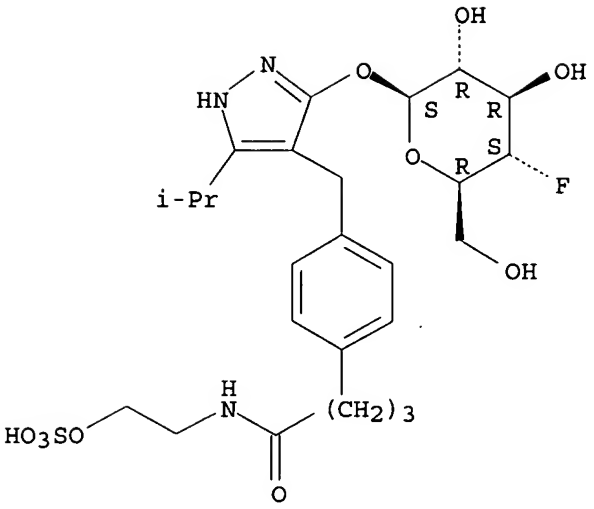
RN 871484-37-6 HCAPLUS
CN Sulfamic acid, [3-[[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



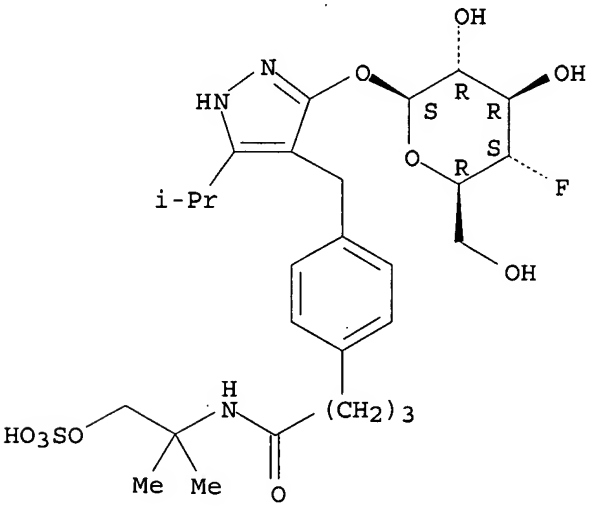
RN 871484-38-7 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-[2-(sulfooxy)ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



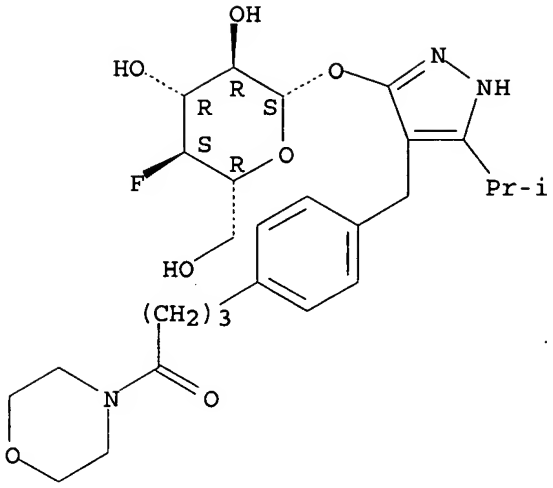
RN 871484-39-8 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-[1,1-dimethyl-2-(sulfooxy)ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



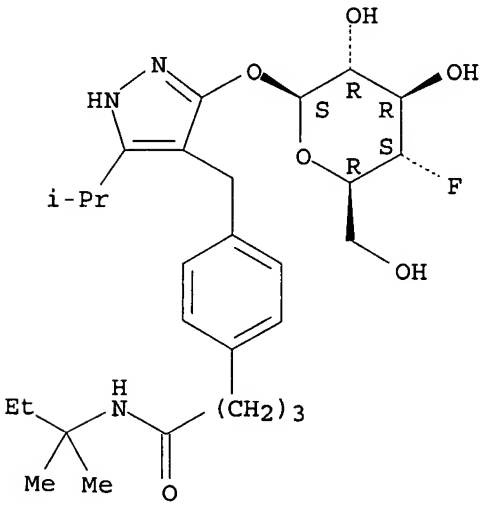
RN 871484-40-1 HCAPLUS
CN Morpholine, 4-[4-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



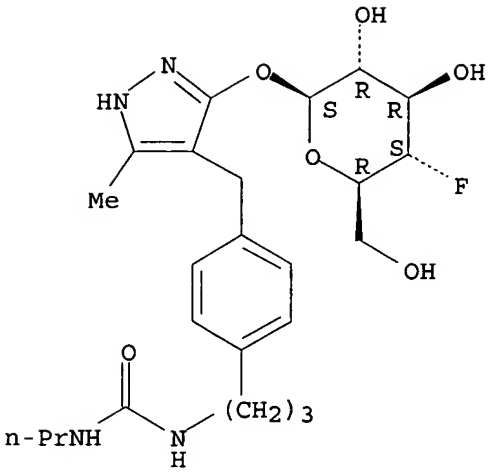
RN 871484-41-2 HCAPLUS
CN Benzenebutanamide, 4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]-N-(1,1-dimethylpropyl)- (CA INDEX NAME)

Absolute stereochemistry.



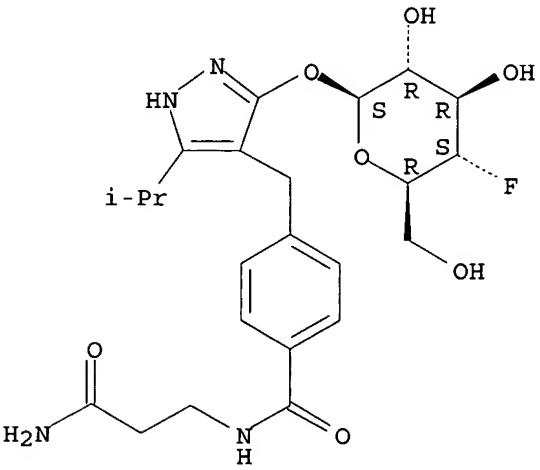
RN 871484-42-3 HCAPLUS
CN Urea, N-[3-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-methyl-1H-pyrazol-4-yl]methyl]phenyl]propyl]-N'-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



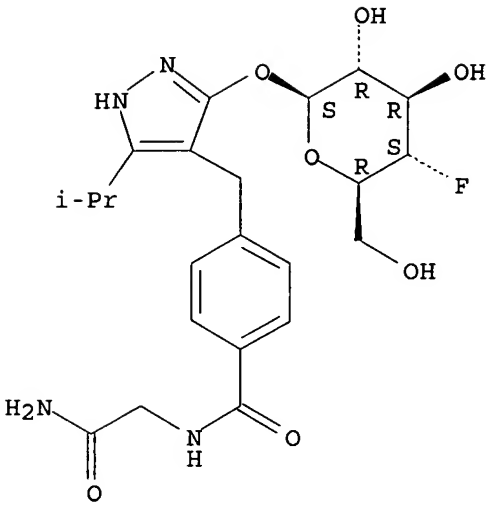
RN 871484-43-4 HCAPLUS
CN Benzamide, N-(3-amino-3-oxopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



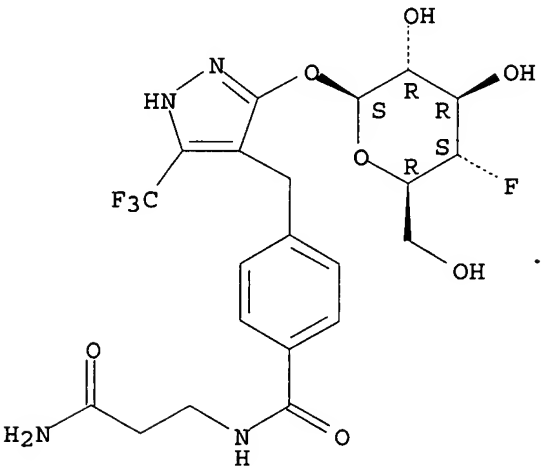
RN 871484-44-5 HCAPLUS
CN Benzamide, N-(2-amino-2-oxoethyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



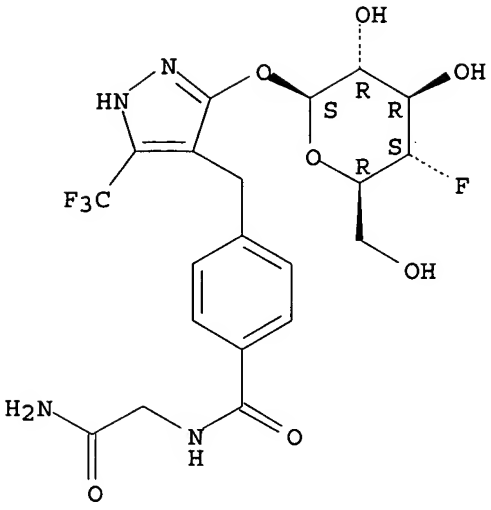
RN 871484-45-6 HCAPLUS
CN Benzamide, N-(3-amino-3-oxopropyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(trifluoromethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



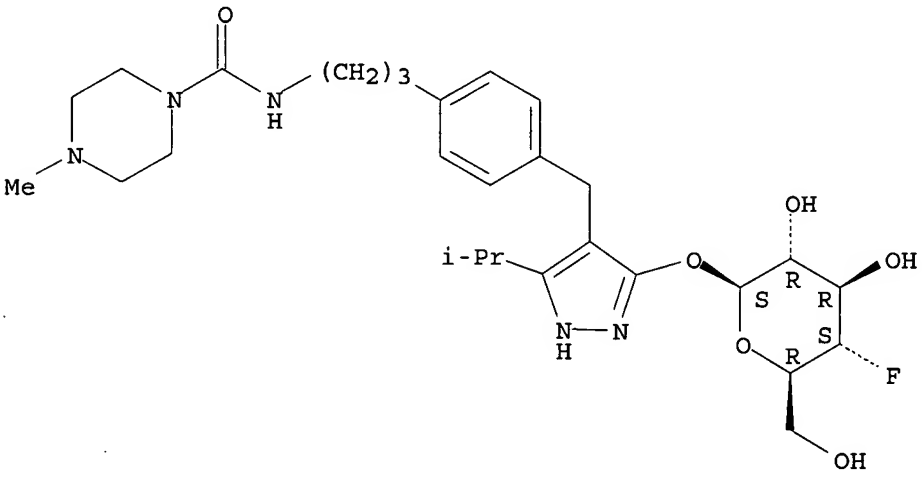
RN 871484-46-7 HCAPLUS
CN Benzamide, N-(2-amino-2-oxoethyl)-4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(trifluoromethyl)-1H-pyrazol-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



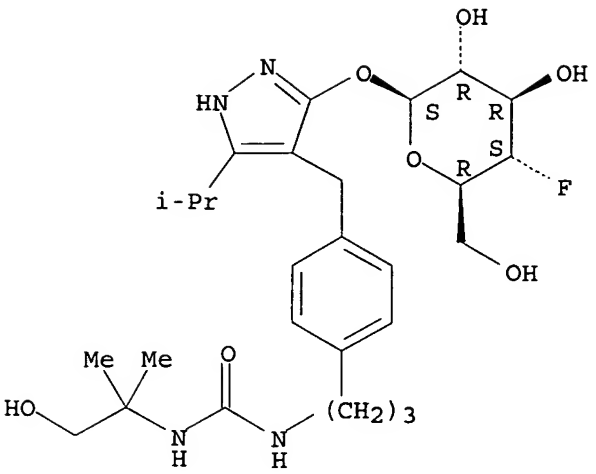
RN 871484-47-8 HCAPLUS
CN 1-Piperazinecarboxamide, N-[3-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]propyl]-4-methyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 871484-48-9 HCAPLUS
CN Urea, N-[3-[4-[[3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(1-methylethyl)-1H-pyrazol-4-yl]methyl]phenyl]propyl]-N'-(2-hydroxy-1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 2005:1328798 HCAPLUS
DN 144:51831
ED Entered STN: 22 Dec 2005
TI Synthesis of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels
IN Brummerhop, Harm; Frick, Wendelin; Glombik, Heiner; Plettenburg, Oliver; Bickel, Martin; Heuer, Hubert; Theis, Stefan
PA Aventis Pharma Deutschland G.m.b.H., Germany
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07H017-02
ICS A61K031-7056; A61P003-10
CC 33-3 (Carbohydrates)
Section cross-reference(s): 1, 25, 28, 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005121161	A1	20051222	WO 2005-EP5959	20050603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2005252329	A1	20051222	AU 2005-252329	20050603
CA 2570042	A1	20051222	CA 2005-2570042	20050603
EP 1758914	A1	20070307	EP 2005-746637	20050603
EP 1758914	B1	20071121		
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CN 1964984	A	20070516	CN 2005-80019067	20050603
BR 2005010770	A	20071120	BR 2005-10770	20050603
US 2007197623	A1	20070823	US 2006-567410	20061206

	KR 2007023726	A	20070228	KR 2006-726083	20061211
	IN 2006CN04531	A	20070629	IN 2006-CN4531	20061211
	NO 2007000176	A	20070309	NO 2007-176	20070110
PRAI	DE 2004-102004028241	A	20040611		
	WO 2005-EP5959	W	20050603		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005121161	ICM	C07H017-02
	ICS	A61K031-7056; A61P003-10
	IPCI	C07H0017-02 [ICM,7]; C07H0017-00 [ICM,7,C*]; A61K0031-7056 [ICS,7]; A61K0031-7042 [ICS,7,C*]; A61P0003-10 [ICS,7]; A61P0003-00 [ICS,7,C*]
	IPCR	A61K0031-7042 [I,C*]; A61K0031-7056 [I,A]; A61P0003-00 [I,C*]; A61P0003-10 [I,A]; C07H0017-00 [I,C*]; C07H0017-02 [I,A]
	ECLA	C07H017/02
DE 102004028241	IPCI	C07H0015-26 [I,A]; A61K0031-7056 [I,A]; A61P0003-10 [I,A]; C07H0017-02 [I,A]; C07H0017-00 [I,C*]; C07H0015-26 [I,A]; C07H0015-00 [I,C*]; A61K0031-7056 [I,A]; A61K0031-7042 [I,C*]; A61P0003-10 [N,A]; A61P0003-00 [N,C*]
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AU 2005252329	IPCI	C07H0017-00 [I,C*]; C07H0017-02 [I,A]
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CA 2570042	IPCI	A61K0031-7056 [I,A]; A61K0031-7042 [I,C*]; A61P0003-10 [I,A]; A61P0003-00 [I,C*]; C07H0017-02 [I,A]; C07H0017-00 [I,C*]
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	ECLA	C07H017/02
EP 1758914	IPCI	C07H0017-02 [I,A]; A61K0031-7056 [I,A]; A61P0003-10 [I,A]; C07H0017-00 [I,C]; A61K0031-7042 [I,C]; A61P0003-00 [I,C]
	IPCR	C07H0017-00 [I,C]; C07H0017-02 [I,A]; A61K0031-7042 [I,C]; A61K0031-7056 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]
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CN 1964984	IPCI	C07H0017-02 [I,A]; C07H0017-00 [I,C*]; A61K0031-7056 [I,A]; A61K0031-7042 [I,C*]; A61P0003-10 [I,A]; A61P0003-00 [I,C*]
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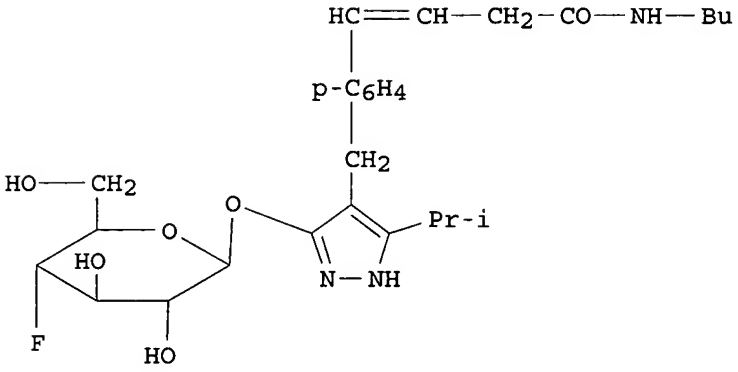
BR 2005010770	IPCI	C07H0017-00 [I,C]; C07H0017-02 [I,A]; A61K0031-7042 [I,C]; A61K0031-7056 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]
	ECLA	C07H017/02
US 2007197623	IPCI	A61K0031-4155 [I,A]; C07D0231-12 [I,A]; C07D0231-00 [I,C*]
	IPCR	A61K0031-4155 [I,C]; A61K0031-4155 [I,A]; A61K0031-7042 [I,C*]; A61K0031-7056 [I,A]; A61P0003-00 [I,C*]; A61P0003-10 [I,A]; C07D0231-00 [I,C]; C07D0231-12 [I,A]; C07H0017-00 [I,C*]; C07H0017-02 [I,A]
	NCL	514/403.000; 548/365.700
	ECLA	C07H017/02
KR 2007023726	IPCI	C07H0017-02 [I,A]; C07H0017-00 [I,A]; A61K0031-7056 [I,A]; A61K0031-7042 [I,C*]; A61P0003-10 [I,A];

A61P0003-00 [I,C*]
IN 2006CN04531 IPCI A61K0031-7056 [ICM,7]; A61K0031-7042 [ICM,7,C*]
NO 2007000176 IPCI C07H0017-00 [I,C]; C07H0017-02 [I,A]
IPCR A61K0031-7042 [I,C*]; A61K0031-7056 [I,A]; A61P0003-00 [I,C*]; A61P0003-10 [I,A]
ECLA C07H017/02
OS MARPAT 144:51831
GI



I

AB The invention relates to substituted fluoro-glycoside derivs. of pyrazoles, e.g. (I), and their physiol. compatible salts, which inhibit Na+-dependent glucose transporter 1 (SGLT-1) and to a method for their production Thus, 1-bromo-4-deoxy-4-fluoro-2,3,6-tri-O-benzoyl-α-D-glucopyranose was prepared from Me 2,3,6-tri-O-benzoyl α-D-galactopyranose in 3 steps, and reacted with 4-(4-bromo-benzyl)-5-isopropylpyraz-3-ol, prepared from Me 4-methyl-3-oxopentanoate in 2 steps, to give the β-linked pyrazole intermediate (II). II was then reacted with 3-butenoic acid, followed by a condensation reaction with n-butylamine and deprotection of the sugar oxygens to give I. In in vitro tests using CHO-TRex-hSGLT1 cell line (derivation given), measuring the concentration at which uptake of Me α-D-glucopyranoside was reduced by 50%, I had IC50 value of 0.043 μM.

ST antidiabetic fluoroglycoside pyrazole deriv prepn SGLT1 inhibitor

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SGLT 1; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT Glycosides
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(fluoro; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT Autoimmune disease
(insulin-dependent diabetes mellitus; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT Diabetes mellitus
(insulin-dependent; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT Diabetes mellitus
(non-insulin-dependent; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT Antidiabetic agents

Fluorination
Human
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT 50-99-7, D-Glucose, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood; preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT 288-13-1P, Pyrazole
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT 871484-07-0P 871484-13-8P 871484-14-9P
871484-15-0P 871484-16-1P 871484-17-2P
871484-18-3P 871484-19-4P 871484-20-7P
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871484-24-1P 871484-25-2P 871484-26-3P
871484-27-4P 871484-28-5P 871484-29-6P
871484-30-9P 871484-31-0P 871484-32-1P
871484-33-2P 871484-34-3P 871484-35-4P
871484-36-5P 871484-37-6P 871484-38-7P
871484-39-8P 871484-40-1P 871484-41-2P
871484-42-3P 871484-43-4P 871484-44-5P
871484-45-6P 871484-46-7P 871484-47-8P
871484-48-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT 77-86-1, Tris(hydroxymethyl)aminomethane 79-10-7, Acrylic acid, reactions 103-76-4, n-(2-Hydroxyethyl)piperazine 109-01-3, n-Methylpiperazine 109-73-9, n-Butylamine, reactions 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 111-49-9, Hexahydro-1H-azepine 123-75-1, Pyrrolidine, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 141-43-5, 2-Aminoethanol, reactions 141-97-9, Ethyl acetoacetate 353-07-1, 2-Cyanoethylhydrazine 372-31-6 589-15-1, 4-Bromobenzyl bromide 594-39-8, tert-Amylamine 619-66-9, 4-Carboxybenzaldehyde 625-38-7, Vinylacetic acid 1668-10-6, Glycinamide hydrochloride 3601-36-3 7152-15-0, Ethylisobutyrylacetate 7803-57-8, Hydrazine hydrate 13961-36-9, 1-Allyl-piperazine 17400-34-9 17768-41-1, 1-Adamantanemethylamine 31166-44-6, Benzyl-1-piperazinecarboxylate 42558-54-3 51642-81-0 64017-81-8, 3-Aminopropionamide hydrochloride 65414-74-6, L-Serinamide hydrochloride 158275-29-7 871484-00-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

IT 84065-98-5P 461025-92-3P 661480-68-8P 702638-17-3P 871484-01-4P
871484-02-5P 871484-03-6P 871484-04-7P 871484-05-8P 871484-06-9P
871484-08-1P 871484-09-2P 871484-10-5P 871484-11-6P 871484-12-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluoro-glycoside derivs. of pyrazoles for use in treatment of diabetes or for lowering blood sugar levels)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aventis Pharma Deutschland Gmbh; WO 2004052903 A 2004 HCAPLUS
(2) Kissei Pharmaceutical Co Ltd; EP 1213296 A 2002 HCAPLUS
(3) Tanabe Seiyaku Co Ltd; EP 0850948 A 1998 HCAPLUS

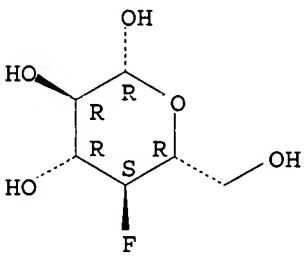
L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:554093 HCAPLUS
DOCUMENT NUMBER: 121:154093
TITLE: Anomeric Dependence of Fluorodeoxyglucose Transport in Human Erythrocytes
AUTHOR(S): O'Connell, Thomas M.; Gabel, Scott A.; London, Robert E.
CORPORATE SOURCE: Laboratory of Molecular Biophysics, National Institute of Environmental Health Sciences, Research Triangle Park, NC, 27709, USA
SOURCE: Biochemistry (1994), 33(36), 10985-92
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The transport of several n-fluoro-n-deoxy-D-glucose derivs. across the human erythrocyte membrane has been studied under equilibrium exchange conditions using one- and two-dimensional NMR (NMR) techniques. This approach is based on the intracellular 19F shift, which was found to depend on the anomeric form and on the F/OH substitution position. Since the transport behavior of both glucose anomers can be followed simultaneously, this approach is particularly sensitive to differences in anomeric permeability. For 2-, 3-, 4-, and 6-fluorodeoxyglucose analogs, the α anomers permeate more rapidly, and the Pα/Pβ ratio is dependent on the position of fluorination, with values of 1.1, 1.3, 2.5, and 1.6, resp., obtained at 37 °C. These results have been analyzed in terms of a simple alternating conformation model for the glucose transporter. Although mutarotase activity has been reported for red cells, mutarotation behavior for all anomers was found to be completely negligible on the transport and spin-lattice relaxation time scales. Metabolic transformation of the fluorinated glucose analogs, primarily to fluorinated gluconate and sorbitol analogs, is very slow and does not significantly interfere with the transport measurements. A mean ratio of 2.6 was found for the extracellular/intracellular fluorine spin-lattice relaxation rates.

IT 27108-04-9 62182-11-0
RL: BIOL (Biological study)
(transport of, by erythrocytes of human, anomeric dependence of)

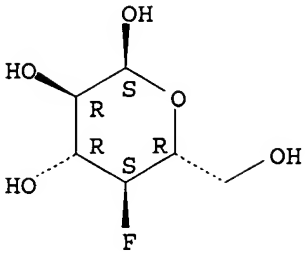
RN 27108-04-9 HCAPLUS
CN β-D-Glucopyranose, 4-deoxy-4-fluoro- (CA INDEX NAME)

Absolute stereochemistry.



RN 62182-11-0 HCAPLUS
CN α-D-Glucopyranose, 4-deoxy-4-fluoro- (CA INDEX NAME)

Absolute stereochemistry.



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      23975279 1800<=PY<=2003
L18          27 L15 AND 1800<=PY<=2003

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L18  ANSWER 1 OF 27  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2003:873375  HCAPLUS
DOCUMENT NUMBER:          140:15550
TITLE:                    Defective P2Y purinergic receptor function: A possible
                          novel mechanism for impaired glucose transport
AUTHOR(S):                Solini, Anna; Chiozzi, Paola; Morelli, Anna; Passaro,
                          Angela; Fellin, Renato; Di Virgilio, Francesco
CORPORATE SOURCE:         Department of Internal Medicine, University of Pisa,
                          Italy
SOURCE:                   Journal of Cellular Physiology (2003),
                          197(3), 435-444
                          CODEN: JCLLAX; ISSN: 0021-9541
PUBLISHER:                Wiley-Liss, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Extracellular ATP is an ubiquitous mediator that regulates several
     cellular functions via specific P2 plasma membrane receptors (P2Rs), for
     which a role in modulating intracellular glucose metab. has been
     recently suggested.  We have investigated glucose uptake in response to
     P2Rs stimulation in fibroblasts from type 2 diabetic (T2D) patients and
     control subjects.  P2Rs expression was evaluated by RT-PCR; intracellular
     calcium release by fluorometry; glucose transporter
     (GLUT1) translocation by immunoblotting and chemiluminescence; glucose
     uptake was measured with 2-deoxy-D-[1-3H]glucose (2-DOG) and ATP by
     luminometry.  Cells from T2D patients, in contrast to those from healthy
     controls, showed no increase in glucose uptake after ATP stimulation;
     extracellular ATP caused, however, a similar GLUT1 recruitment to the
     plasma membrane in both groups.  P2Rs expression did not differ between
     fibroblasts from diabetic and healthy subjects, but while plasma membrane
     depolarization, a P2X-mediated response was similar in both groups, no
     evident intracellular calcium increase was detectable in the cells from
     the former group.  The calcium response in fibroblasts from diabetics was
     restored by co-incubation with apyrase or hexokinase, suggesting that
     P2YRs in those cells were normally expressed but chronically desensitized.
     In support to this finding, fibroblasts from T2D subjects secreted a
     two-fold larger amount of ATP compared to controls.  Pre-treatment with
     apyrase or hexokinase also restored ATP stimulated glucose uptake in
     fibroblasts from diabetic subjects.  These results suggest that
     extracellular ATP plays a role in the modulation of glucose
     transport via GLUT1, and that the P2Y-dependent GLUT1 activation
     is deficient in fibroblasts from T2D individuals.  Our observations may
     point to addnl. therapeutic targets for improving glucose utilization in
     diabetes.
RN   50-99-7
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RN 56-65-5
RN 7440-70-2
RN 9004-10-8
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:757208 HCAPLUS
DOCUMENT NUMBER: 137:273386
TITLE: Monitoring of tumour glucose metabolism by PET in a phase I study evaluating hormonal therapy in advanced pancreatic cancer
AUTHOR(S): Eckel, F.; Lersch, C.; Lippl, F.; Schulte-Frohlinde, E.; Schusdziarra, V.; Helmberger, H.; Neverve, J.; Decker, M.; Frank, R.; Schwaiger, M.; Weber, W.
CORPORATE SOURCE: Depts. of Medicine II, Diagnostic Radiology, Nuclear Medicine, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany
SOURCE: Scandinavian Journal of Gastroenterology (2002), 37(8), 972-977
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Positron emission tomog. (PET) dets. therapy-induced changes in tumor glucose utilization. Exptl. data indicate that cholecystokinin (CCK) stimulates pancreatic cancer growth. In this study in patients with advanced pancreatic cancer, we evaluated the use of fluorodeoxy-glucose (FDG) PET compared with magnetic resonance imaging (MRI) in monitoring hormonal therapy using a highly selective, non-peptide CCK receptor antagonist (SR 27897B). Nineteen patients were enrolled on a 28-day course of SR 27897B. Initially, 4 patients received 20 mg of SR 27897B; 9 patients received 40 mg; and 6 patients 80 mg. Imaging studies, including FDG-PET and MRI, were performed at baseline and on days 14 and 28. No significant changes in FDG uptake by the primary tumors were observed Rate of progression of disease was 11 (61 %) of 18 evaluable patients by MRI. Median survival of all patients enrolled was 2.7 mo. SR 27897B was fairly well tolerated at all doses tested. The most common side effects were gastrointestinal disorders such as diarrhea, flatulence and nausea. SR 27897B, when used alone at the limited doses employed, led neither to an impairment of tumor glucose metab. nor to a reduction of tumor size in advanced pancreatic cancer.
RN 136381-85-6
RN 29702-43-0
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:763028 HCAPLUS
DOCUMENT NUMBER: 135:315589
TITLE: Measurement of nutrient uptake in cells and methods based thereon
INVENTOR(S): Friederich, Srienc; Natarajan, Arvind; Abu-Absi, Nicholas R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001077140	A2	20011018	WO 2000-US28913	20001019 <--
WO 2001077140	A3	20020221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001059015	A5	20011023	AU 2001-59015	20001019 <--
PRIORITY APPLN. INFO.:			US 1999-160335P	P 19991019
			WO 2000-US28913	W 20001019

AB The fluorescent glucose analog, 2-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-2-deoxyglucose (2-NBDG), was used to measure rates of glucose uptake by single Escherichia coli cells. When cell populations were exposed to the glucose analog, the sugar was actively transported and accumulated in single cells to a steady-state level that depended upon the extracellular concentration of the sugar, the sugar transport capacity of the cells, and the intracellular degradation rate. The dependence upon substrate concentration could be described according to Michaelis-Menten kinetics with apparent saturation constant KM=1.75 μM, and maximum uptake rate = 197 mols./cell-second. Specificity of glucose transporters to the analog was confirmed by inhibition of uptake of 2-NBDG by D-glucose, 3-o-Me glucose, and D-glucosamine, and lack of inhibition by L-glucose. The assay for sugar uptake is extremely sensitive such that the presence of even trace amts. of D-glucose in the culture medium (.apprx.0.2 μM) is detectable. The rates of single-cell sugar uptake were found to increase differentially with cell size as measured by microscopy or single-cell light scattering intensity. A math. model was developed to provide a theor. basis for estimating single-cell glucose uptake rates from single-cell 2-NBDG uptake rates. Because the distribution of single-cell sugar uptake rates of the entire cell population is measured, this assay provides a novel means of estimating the instantaneous rates of nutrient depletion in the culture medium.

RN 186689-07-6
RN 108708-22-1
RN 50-99-7
RN 57-48-7
RN 57-50-1
RN 58-86-6
RN 63-42-3
RN 69-79-4
RN 634-74-2
RN 3458-28-4
RN 146-72-5
RN 3416-24-8

L18 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	1998:146121 HCAPLUS
DOCUMENT NUMBER:	128:241328
TITLE:	Glucose transporter protein-independent tumor cell accumulation of fluorine-18-AFDG, a lipophilic fluorine-18-FDG analog
AUTHOR(S):	Waki, Atsuo; Fujibayashi, Yasuhisa; Magata, Yasuhiro; Yokoyama, Akira; Sadato, Norihiro; Tsuchida, Tatsuro; Ishii, Yasushi; Yonekura, Yoshiharu
CORPORATE SOURCE:	Biomedical Imaging Research Center, Fukui Medical School, Fukui, 910-11, Japan
SOURCE:	Journal of Nuclear Medicine (1998), 39(2), 245-250

CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluorine-18-fluorodeoxyglucose (FDG) is used clin. for tumor diagnosis, but its mechanism of accumulation in tumor cells is complicated because two factors, glucose transporter protein (GLUT) and hexokinase, govern [18F]FDG uptake directly. We selected a lipophilic [18F]FDG analog, 1,3,4,6-tetra-acetyl-2-[18F]-2-deoxy-D-glucose ([18F]AFDG), to regulate the effects of hexokinase and evaluated its characteristics in an in vitro cell culture system. Fluorine-18-AFDG was synthesized by the method used to produce [18F]FDG, as an intermediate of [18F]FDG. Fluorine-18-AFDG uptake study was performed with LS180 tumor cells, and its metabolites were also investigated by thin-layer chromatog. To evaluate the relationship between [18F]AFDG and GLUT, we also examined [18F]AFDG uptake in the presence of cytochalasin B or with increased medium glucose concentration The effects of lowered temperature (4°C) on [18F]AFDG uptake were also investigated. Fluorine-18-AFDG (lipophilicity: octanol/water = 3.5) uptake was 3.3-fold higher than that of [18F]FDG. Metabolic anal. showed that [18F]AFDG was extremely stable in the incubation medium but was quickly hydrolyzed and metabolized to 2-fluoro-[18F]-2-deoxy-D-glucose-6-phosphate ([18F]FDG-6P) in tumor cells. Fluorine-18-FDG-6P accounted for approx. 45% of the total radioactivity after a 60-min incubation of [18F]AFDG. Incubation with 50 μM cytochalasin B did not affect [18F]AFDG uptake. In medium with double the control glucose level, [18F]FDG uptake was decreased by about 50%, but [18F]AFDG uptake was not affected. Fluorine-18-AFDG uptake and [18F]FDG-6P production did not show saturation and increased linearly with addition of a 10-fold higher concentration of [18F]AFDG. Lowered incubation temperature caused decreased [18F]AFDG uptake due to reduced [18F]FDG-6P production Fluorine-18-AFDG rapidly penetrated the cell membrane as a result of its high lipophilicity and was metabolized to [18F]FDG-6P within cells. Fluorine-18-AFDG was thus characterized as "GLUT-independent [18F]FDG.".
RN 63503-12-8
RN 128441-61-2P
RN 106984-34-3
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:594806 HCAPLUS
DOCUMENT NUMBER: 123:51535
TITLE: Fundamental limitations of [18F]2-deoxy-2-fluoro-D-glucose for assessing myocardial glucose uptake
AUTHOR(S): Hariharan, Ramesh; Bray, Molly; Ganim, Ricky; Doenst, Torsten; Goodwin, Gary W.; Taegtmeyer, Heinrich
CORPORATE SOURCE: Medical School, University of Texas, Houston, TX, 77030, USA
SOURCE: Circulation (1995), 91(9), 2435-44
CODEN: CIRCAZ; ISSN: 0009-7322
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The glucose tracer analog [18F]2-deoxy-2-fluoro-D-glucose (FDG) is widely used for assessing regional myocardial glucose metab. in vivo. The reproducibility of this method has recently been questioned because of a discordant affinity of hexokinase for its substrates glucose and 2-deoxyglucose. The authors therefore compared rates of glucose utilization simultaneously with tissue time-activity curves of FDG uptake before and after changes in the physiol. environment of the heart. Methods and Results Isolated working rat hearts were perfused for 60 min with recirculating Krebs buffer containing glucose (10 mmol/L), FDG (1 μCi/mL), [2-3H]glucose (0.05 μCi/mL), and [U-14C]2-deoxyglucose (2-DG; 0.025 μCi/mL). Myocardial glucose uptake was measured by tracer

([2-3H]glucose) and tracer analog methods (FDG and 2-DG) before and after the addition of either insulin (1 mU/mL), epinephrine (1 μmol/L), lactate (40 mmol/L), or d,l-β-hydroxybutyrate (40 mmol/L) at 30 min of perfusion and after acute changes in cardiac workload. Under steady-state conditions, myocardial rates of glucose utilization as measured by tritiated water (3H2O) production from metab. of [2-3H]glucose, FDG uptake, and 2-DG retention were linearly related. The addition of competing substrates decreased glucose utilization immediately. The addition of insulin increased the rate of glucose utilization as measured by the glucose tracer but not as measured by the tracer analogs. The ratio of 3H2O release/myocardial FDG uptake increased by 111% after the addition of insulin, by 428% after the addition of lactate, and by 232% after the addition of β-hydroxybutyrate. Epinephrine increased rates of glucose utilization and contractile performance, whereas there was no increase in glucose uptake with a comparable increase in workload alone. There was no change in the relation between the glucose tracer and the tracer analog either with epinephrine or with acute changes in workload. The uptake and retention of FDG in heart muscle is linearly related to glucose utilization only under steady-state conditions. Addition of insulin or of competing substrates changes the relation between uptake of the glucose tracer and FDG. These observations preclude the determination of absolute rates of myocardial glucose uptake by the tracer analog method under non-steady-state conditions.

RN 50-99-7
RN 63503-12-8

L18 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:431706 HCAPLUS
DOCUMENT NUMBER: 121:31706
TITLE: Regional differences in glucose transport in the mouse hippocampus
AUTHOR(S): Shimada, Masahisa; Kawamoto, Seiichi; Hirose, Yayoi; Nakanishi, Masatomo; Watanabe, Hirotoshi; Watanabe, Masahito
CORPORATE SOURCE: Dep. Anat., Osaka Med. Coll., Takatsuki, 569, Japan
SOURCE: Histochemical Journal (1994), 26(3), 207-12
CODEN: HISJAE; ISSN: 0018-2214
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to observe glucose transport into the brain, 6-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino]-6-deoxyglucose (NBDG), a non-metabolizable and fluorescent glucose analog, was injected i.v. into mice. After ascertaining that this glucose analog is non-metabolizable in the brain, the NBDG contents in the blood and brain were measured quant. by spectrofluorimetry at 0, 0.5, 2, 5, 10 and 30 min after i.v. injection. The NBDG content in the blood decreased markedly with time, whereas in the brain it rapidly decreased, then gradually increased after 2 min. Glucose transport into the hippocampus was observed with a confocal laser scanning microscope. At 0.5 min, NBGD was seen to be highly concentrated on the vascular wall. Using the confocal mode, it was found that the fluorescence was unevenly distributed on the microvessel wall, suggesting local differences of glucose transport in the vascular wall. At 5 min, the fluorescent intensity of the vascular wall was markedly decreased, whereas relatively intense fluorescence was observed in the cerebral parenchyma of the stratum lacunosum-moleculare and stratum pyramidale of CA3. At 10 min, a weak fluorescence was diffusely distributed in the hippocampus. As to the localization of NBDG in the brain, capillary endothelium (luminal and abluminal membrane), basement membrane, and the feet of the astrocytes are discussed.

RN 50-99-7

L18 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:293349 HCAPLUS
DOCUMENT NUMBER: 120:293349
TITLE: Internalization and sorting of a fluorescent analog of glucosylceramide to the Golgi apparatus of human skin fibroblasts: utilization of endocytic and nonendocytic transport mechanisms
AUTHOR(S): Martin, Ona C.; Pagano, Richard E.
CORPORATE SOURCE: Dep. Embryol., Carnegie Inst. Washington, Baltimore, MD, 21210-3399, USA
SOURCE: Journal of Cell Biology (1994), 125(4), 769-81
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors examined the uptake and intracellular transport of the fluorescent glucosylceramide analog N-[5-(5,7-di-Me BODIPY)-1-pentanoyl]-glucosyl sphingosine (C5-DMB-GlcCer) in human skin fibroblasts and compared its behavior to that of the corresponding fluorescent analogs of sphingomyelin, galactosylceramide, and lactosylceramide. All 4 fluorescent analogs were readily transferred from defatted BSA to the plasma membrane during incubation at 4°. When cells treated with C5-DMB-GlcCer were washed, warmed to 37°, and subsequently incubated with defatted BSA to remove fluorescent lipid at the cell surface, strong fluorescence was observed at the Golgi apparatus, as well as weaker labeling at the nuclear envelope and other intracellular membranes. Similar results were obtained with C5-DMB-galactosylceramide, except that labeling of the Golgi apparatus was weaker than with C5-DMB-GlcCer. Internalization of C5-DMB-GlcCer was not inhibited by various treatments, including ATP depletion or warming to 19°, and biochem. anal. demonstrated that the lipid was not metabolized during its internalization. However, accumulation of C5-DMB-GlcCer at the Golgi apparatus was reduced when cells were treated with a nonfluorescent analog of glucosylceramide, suggesting that accumulation of C5-DMB-GlcCer at the Golgi apparatus was a saturable process. In contrast, cells treated with C5-DMB-analogs of sphingomyelin or lactosylceramide internalized the fluorescent lipid into a punctate pattern of fluorescence during warming at 37°, and this process was temperature and energy dependent. These results with C5-DMB-sphingomyelin and C5-DMB-lactosylceramide were analogous to those obtained with another fluorescent analog of sphingomyelin in which labeling of endocytic vesicles and plasma membrane lipid recycling were documented (Koval, M.; Pagano, R. E., 1990). Incubation of perforated cells with C5-DMB-sphingomyelin resulted in prominent labeling of the nuclear envelope and other intracellular membranes, similar to the pattern observed with C5-DMB-GlcCer in intact cells. These observations are consistent with the transbilayer movement of fluorescent analogs of glucosylceramide and galactosylceramide at the plasma membrane and early endosomes of human skin fibroblasts and suggest that both endocytic and nonendocytic pathways are used in the internalization of these lipids from the plasma membrane.
RN 4682-48-8
RN 85305-87-9
RN 85305-88-0
RN 133867-54-6

L18 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:3120 HCAPLUS
DOCUMENT NUMBER: 118:3120
TITLE: Comparison of regional blood-brain transport kinetics between glucose and fluorodeoxyglucose
AUTHOR(S): Lear, James L.; Ackerman, Robert F.
CORPORATE SOURCE: Health Sci. Cent., Univ. Colorado, Denver, CO, USA
SOURCE: Journal of Nuclear Medicine (1992), 33(10), 1819-24

CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fluorodeoxyglucose (FDG) method for estimating regional cerebral glucose metabolic rate (LCMRglc) requires that a fixed relationship (the "lumped constant") exists between net FDG and glucose (GLC) extraction throughout the brain. In addition to the relative rate of metab. between FDG and GLC, this assumed constant is affected by the relative rate of blood-to-brain FDG transport compared to that of glucose. However, little data is available regarding the regional stability of the FDG vs. GLC transport-rate relationship. High resolution, quant. dual-tracer digital autoradiog. was therefore used to directly compare the blood-to-brain transport rate consts. (K1) of radiolabeled GLC and FDG in normal and pharmacol.-stimulated rats. The rats were given 45 s terminal i.v. infusions of a mixture of 18F-FDG and 14C-GLC. Autoradiograms of the brain representing the FDG and GLC tracer concns. were produced, digitized, and converted into digital images of K1. The global K1 values of FDG and GLC were not different from each other. However, detailed anal. revealed that some structures in the normal animals, such as the hippocampus and cerebellum, had different quant. patterns of FDG transport compared to GLC transport. The relation between GLC and FDG transport is not uniform throughout the brain as has previously been assumed. Regional variations in the type and distribution of glucose transporters may exist and the fluorodeoxyglucose "lumped constant" may vary somewhat among different brain regions.
RN 50-99-7
RN 815-92-9
RN 63503-12-8

L18 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:17899 HCAPLUS
DOCUMENT NUMBER: 116:17899
TITLE: Differential spectrofluorometry in the human vitreous: blood-retina barrier permeability to fluorescein and fluorescein glucuronide
AUTHOR(S): Larsen, Michael; Dalgaard, Peter; Lund-Andersen, Henrik
CORPORATE SOURCE: Dep. Ophthalmol., Gentofte Hosp., Hellerup, DK-2900, Den.
SOURCE: Graefe's Archive for Clinical and Experimental Ophthalmology (1991), 229(4), 350-7
CODEN: GACODL; ISSN: 0721-832X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method is described for the sep. quantitation of fluorescein and fluorescein glucuronide in the vitreous by differential spectrofluorometry. An ocular fluorometer was equipped with monochromatic laser excitation at two rapidly interchangeable wavelengths. The data anal. accounts for absorption of light in the cornea, lens, and extrinsic ocular fluorophores. Examination of seven patients with insulin-dependent diabetes and different degrees of diabetic retinopathy demonstrated that both fluorescein and fluorescein glucuronide enter the eye through the blood-retina barrier. The mean ratio between the permeabilities of fluorescein glucuronide and fluorescein was 0.9 (range, 0.3-1.9). Thus, differences in the mol. size and lipid solubility of the two substances appear to be of little or no importance for their inward penetration of the barrier. No association was found between the relative permeability and the degree of retinopathy.
RN 2321-07-5
RN 74804-84-5

L18 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:139356 HCAPLUS
DOCUMENT NUMBER: 114:139356
TITLE: The loss of fluorescein, fluorescein glucuronide and fluorescein isothiocyanate dextran from the vitreous by the anterior and retinal pathways
AUTHOR(S): Araie, M.; Maurice, D. M.
CORPORATE SOURCE: Med. Cent., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Experimental Eye Research (1991), 52(1), 27-39
CODEN: EXERA6; ISSN: 0014-4835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pathways by which fluorescein (F), fluorescein glucuronide (FG) and fluorescein dextran (FD) leave the vitreous body of the rabbit were examined by measuring the concentration distribution of the injected fluorophores in sections of the frozen eyes. The contours of F as already known, show that it leaves the vitreous predominantly across the retinal surface. Math. anal. of the concentration gradient leads to an average outward permeability coefficient of 1.4 + 10-3 cm min-1 for the retinal layers. The contours of FG and FD show that they leave predominantly by diffusion into the posterior chamber, encountering only a minor barrier at the anterior hyaloid membrane. The anterior contours indicate that there can be no substantial posteriorly directed fluid flow through the vitreous; if it occurs its velocity across the retinal surface must be less than 2 + 10-5 cm min-1. The contours of FD near the posterior pole of the retina suggest that such a flow may be taking place. Some time after the systemic administration of F, an anal. of the rate of loss of fluorescence from the vitreous body shows that this corresponds to the movement of FG out through the anterior chamber. Its value bears little relationship to the condition of the blood-vitreal barrier.
RN 2321-07-5
RN 60842-46-8
RN 74804-84-5

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L18 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:34018 HCAPLUS
DOCUMENT NUMBER: 110:34018
TITLE: Fluorescein-labelled glucagon: a new probe for the study of receptor disposition in membranes
AUTHOR(S): Cantrill, Richard C.; Ward, Larry W.; Heithier, Helmuth; Klein, Helmut W.; Peters, Reiner; Helmreich, Ernst J. M.
CORPORATE SOURCE: Physiol.-Chem. Inst., Univ. Wuerzburg, Wuerzburg, 8700, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1988), 92(9), 973-8
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New fluorescent glucagon derivs. were synthesized by converting tryptophan25 to 2-thiol-tryptophan and the subsequent use of thiol-specific fluorescent reagents. All derivs. retained the ability to bind tightly to rat liver membranes and rat hepatocytes in primary culture and to activate adenylate cyclase as potently as native glucagon. Thus these derivs. are full agonists. From expts. with monolayer cultured hepatocytes and 125I-labeled glucagon at elevated temps. it was assumed that the ligand was internalized at this temperature since some of the specifically bound ligand could no longer be washed off with acid. This was confirmed in expts. where monolayer cultures of hepatocytes were

incubated with the fluorescein-labeled derivs. of glucagon, thus allowing the study of the distribution of glucagon specifically bound on the cell surface using video intensification microscopic techniques. In keeping with autoradiog. studies using radiolabeled glucagon, or electron microscope studies using ferritin-labeled glucagon, it can now be shown using fluorescently labeled glucagon derivs. and video intensification microscopy that at lower temps. the bound ligand was distributed all over the cell surface. At higher temps., however, ligand-derived fluorescence could only be detected in mobile intracellular vesicles following internalization and removal from the cell surface.

RN 68169-37-9
RN 9012-42-4
RN 9007-92-5DP
RN 118215-97-7P
RN 118215-99-9P
RN 118216-00-5P
RN 118216-06-1P
RN 118216-09-4P
RN 75807-95-3

L18 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:129073 HCAPLUS
DOCUMENT NUMBER: 108:129073
TITLE: Movement of fluorescein and fluorescein glucuronide across the isolated rabbit iris-ciliary body
AUTHOR(S): Eguchi, Shuichiro; Araie, Makoto; Takase, Masahiro
CORPORATE SOURCE: Sch. Med., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Japanese Journal of Ophthalmology (1987), 31(3), 440-54
CODEN: JJOPA7; ISSN: 0021-5155
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Movement of fluorescein and fluorescein glucuronide, a fluorescent metabolite of fluorescein, across the isolated iris-ciliary body of the albino rabbit was determined under short-circuit conditions by using a modified Ussing's chamber. The permeabilities of this tissue to these dyes were calculated The outward permeability (from the aqueous to the stromal side) of the iris-ciliary body preparation averaged 6.63 for fluorescein and 1.51 + 10-6 cm/s for fluorescein glucuronide, and the inward permeability (from the stromal to the aqueous side) was 1.68 for fluorescein and 1.37 + 10-6 cm/s for fluorescein glucuronide, resp. Application of probenecid or ouabain decreased the outward permeability of fluorescein, but it had no significant effect on the fluorescein glucuronide movement. Application of 10-5 M 2,4-dinitrophenol showed no significant effect on the fluorescein or fluorescein glucuronide movement, but application of 5 + 10-4 M 2,4-dinitrophenol decreased the outward fluorescein transfer, which was also markedly suppressed by incubation at 0°. It is possible that an active transport mechanism is involved in the outward fluorescein movement across the iris-ciliary body, while the inward movement of fluorescein and also the fluorescein glucuronide movement across this tissue is mainly by passive diffusion.

RN 2321-07-5
RN 74804-84-5

L18 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:614334 HCAPLUS
DOCUMENT NUMBER: 107:214334
TITLE: Human corneal endothelial permeability to fluorescein and fluorescein glucuronide

AUTHOR(S): Seto, Chihiro; Araie, Makoto; Sawa, Mitsuru; Takase, Masahiro
CORPORATE SOURCE: Sch. Med., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Investigative Ophthalmology & Visual Science (1987), 28(9), 1457-63
CODEN: IOVSDA; ISSN: 0146-0404
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The corneal endothelial permeability coefficient (Pac) for fluorescein (I) and fluorescein glucuronide (II) was determined in normal young volunteers. After oral administration of fluorescein, the apparent concns. of both dyes in the corneal stroma and the anterior chamber were measured by differential fluorometry. The apparent dye levels calculated directly from the in vivo fluorometric measurements were converted to the true ones, based on the result of a normalization experiment performed in rabbit eyes. The value of Pac averaged 5.44 + 10-4 cm/min for I and 3.77 + 10-4 cm/min for II. The aqueous-cornea distribution ratio was 0.50 for I and 0.66 for II. The previously reported values of Pac for I in the human eye may have been underestimates.
RN 518-47-8D
RN 518-47-8
RN 2321-07-5

L18 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:508774 HCAPLUS
DOCUMENT NUMBER: 107:108774
TITLE: Analysis of transport of fluorescein derivatives in the ocular tissue. II. Intraocular behavior of intravenously administered fluorescein glucuronide
AUTHOR(S): Hara, Keiko; Miyake, Kensaku; Iwata, Shuzo
CORPORATE SOURCE: Shohzankai Med. Found., Miyake Eye Hosp., Nagoya, 462, Japan
SOURCE: Atarashii Ganka (1987), 4(2), 270-2
CODEN: ATGAEX; ISSN: 0910-1810
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Fluorescein glucuronide, injected i.v. into rabbits, was found as free fluorescein in the retinal pigment epithelium-choroid, iris, ciliary body, and sensory retina 3 or 5 h after injection, but not in 2 h aqueous humor and the vitreous body. This phenomenon can be used as a measurement of the ability of ocular tissues to excrete foreign compds. into the circulation.
RN 2321-07-5D

L18 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:78730 HCAPLUS
DOCUMENT NUMBER: 106:78730
TITLE: Effect of fluoride on uptake of D-glucose by isolated epithelial cells of rat intestine
AUTHOR(S): Shayiq, R. M.; Kidwai, A. M.
CORPORATE SOURCE: Ind. Toxicol. Res. Cent., Lucknow, 226001, India
SOURCE: Environmental Research (1986), 41(2), 388-99
CODEN: ENVRAL; ISSN: 0013-9351
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Inhibition of the uptake of D-glucose [50-99-7] by isolated intestinal epithelial cells (IIEC) was observed with F- at concns. between 0.25 and 5 mM. Active transport was almost completely inhibited at 5 mM. When CaCl2 was added to F- solution, the inhibitory effect on glucose uptake was abolished. Preincubation of IIEC with different concns. of F- (2.5-5.0 mM) for different intervals of time (2-20 min) at different pH levels (6.2-7.8) and temps. (0-37°) revealed that the conditions

which led to higher uptake of F- by IIEC produced maximum inhibition. The degree of inhibition was not appreciably altered by a change in glucose concns. A concentration-dependent effect of F- on lactic acid [50-21-5] and CO2 production by IIEC was also observed
RN 10043-52-4
RN 50-21-5
RN 124-38-9
RN 16984-48-8
RN 50-99-7

L18 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:164736 HCAPLUS
DOCUMENT NUMBER: 104:164736
ORIGINAL REFERENCE NO.: 104:26001a,26004a
TITLE: Study of fluorescein glucuronide. II. A comparative ocular kinetic study of fluorescein and fluorescein glucuronide
AUTHOR(S): Seto, C.; Araie, M.; Takase, M.
CORPORATE SOURCE: Sch. Med., Univ. Tokyo, Tokyo, Japan
SOURCE: Graefe's Archive for Clinical and Experimental Ophthalmology (1986), 224(2), 113-17
CODEN: GACODL; ISSN: 0721-832X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Comparative studies of fluorescein and fluorescein glucuronide were done. Binding to human serum protein was studied by using an Amicon MPS-3 ultrafiltration unit, it averaged 63% for fluorescein glucuronide and 85% for fluorescein. Intracameral penetration of both compds. was studied in the human eye, and the concentration changes of both compds. in the plasma ultrafiltrate and in the anterior chamber were analyzed, based on Davson's equation. The coefficient of entry into the anterior chamber (ki) was 0.018 h-1 for fluorescein glucuronide and 0.054 h-1 for fluorescein. The rate of loss from the vitreous (kv) was studied by injecting each compound into the vitreous of the pigmented rabbit and following the fluorescein intensity changes in it. It was 0.042 h-1 for fluorescein glucuronide and 0.17 for fluorescein. I.p. injection of probenecid significantly decreased the kv of fluorescein but had little effect that of fluorescein glucuronide. Apparently, fluorescein glucuronide is lost from the vitreous mainly by a passive mechanism.
RN 74804-84-5
RN 2321-07-5
RN 57-66-9

L18 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:3801 HCAPLUS
DOCUMENT NUMBER: 104:3801
ORIGINAL REFERENCE NO.: 104:695a,698a
TITLE: A reevaluation of corneal endothelial permeability to fluorescein
AUTHOR(S): Araie, Makoto; Maurice, David M.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Stanford, CA, USA
SOURCE: Experimental Eye Research (1985), 41(3), 383-90
CODEN: EXERA6; ISSN: 0014-4835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The permeability of the corneal endothelium and its aqueous-cornea distribution ratio were reevaluated in the rabbit eye. Both parameters were determined in an individual eye by applying the dye first by iontophoresis and then by intravitreal injection, which allows the influence of fluorescein glucuronide on the fluorophotometric

measurements to be excluded. The corneal endothelial permeability coefficient was 5.13 + 10-4 cm/min, and the aqueous-cornea distribution ratio was 0.25 on the average, and the former was considerably greater than the previous results, although the latter was considerably smaller.

L18 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:93513 HCAPLUS
DOCUMENT NUMBER: 102:93513
ORIGINAL REFERENCE NO.: 102:14663a,14666a
TITLE: Intracellular translocation of fluorescent sphingolipids in cultured fibroblasts: endogenously synthesized sphingomyelin and glucocerebroside analogs pass through the Golgi apparatus en route to the plasma membrane
AUTHOR(S): Lipsky, Naomi; Pagano, Richard E.
CORPORATE SOURCE: Dep. Embryol., Carnegie Inst. Washington, Baltimore, MD, 21210, USA
SOURCE: Journal of Cell Biology (1985), 100(1), 27-34
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When monolayer cultures of Chinese hamster lung fibroblasts are briefly incubated at 2° with the fluorescent sphingolipid analog C6-NBD-ceramide (N-[7-(4-nitrobenzo-2-oxa-1,3-diazole)]aminocaproyl sphingosine), fluorescent labeling of the mitochondria, endoplasmic reticulum, and nuclear envelope occur. During further incubation at 37°, the Golgi apparatus, and later the plasma membrane, become intensely fluorescent. Within this period, the C6-NBD-ceramide is converted to equal amts. of fluorescent sphingomyelin and glucocerebroside (Lipsky, N. G.; Pagano, R. E., 1983). In the present study, the intracellular translocation of these metabolites and their subsequent appearance at the plasma membrane were investigated by fluorescence microscopy, the addition of the ionophore monensin, and the technique of back exchange, in which the amts. and types of fluorescent lipids present at the cell surface are identified after their transfer from the cell surface into recipient vesicles. In control cells, the amount of fluorescent glucocerebroside and sphingomyelin that could be removed from the cell surface by back exchange increased during incubation at 37°, correlating with the increased fluorescence of the plasma membrane observed by microscopy. In the presence of 10 μM monensin, visible labeling of the plasma membrane was greatly diminished, whereas the Golgi apparatus became highly fluorescent and distended. The ability to remove fluorescent metabolites from the cell surface by back exchange was significant but reversibly inhibited by monensin. Monensin also increased the total amount of fluorescent sphingomyelin, but not the glucocerebroside found in cells. Subcellular fractions were assayed for their ability to convert radiolabeled and fluorescent ceramides to the corresponding sphingomyelins and glucocerebrosides. The activities of parallel fractions coincided, suggesting that the presence of the NBD moiety did not affect the cellular metab. of ceramide. Furthermore, the major peak of sphingomyelin- and glucocerebroside-synthesizing activity appeared to coincide with an enriched Golgi fraction. Apparently, fluorescent sphingomyelin was not synthesized at the plasma membrane, as has recently been suggested for endogenous sphingomyelin. Rather, both the sphingomyelin and glucocerebroside analogs were synthesized intracellularly from C6-NBD-ceramide and translocated through the Golgi apparatus to the cell surface.
RN 94885-03-7
RN 94885-04-8
RN 94885-02-6P

L18 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:72386 HCAPLUS
DOCUMENT NUMBER: 102:72386
ORIGINAL REFERENCE NO.: 102:11215a,11218a
TITLE: The effects of fluorescein monoglucuronide on the calculation of the diffusion transfer coefficient (kdpa) in the blood-aqueous barrier after systemic administration of fluorescein
AUTHOR(S): Seto, Chihiro; Araie, Makoto; Takase, Masahiro; Minoda, Kensei
CORPORATE SOURCE: Fac. Med., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Nippon Ganka Gakkai Zasshi (1984), 88(12), 1572-80
CODEN: NGZAA6; ISSN: 0029-0203
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The average values of transfer coeffs. of fluorescein (F) [2321-07-5] and fluorescein monoglucuronide (FG) [74804-84-5] across the blood-aqueous humor barrier of the human eye were 0.45 + 10-3/min for F and 0.40 + 10-3/min for FG+F after i.v. injection of 10% fluorescein Na. However, the values after oral administration at the same dose were 1.0 and 0.8 + 10-3/min for F and FG + F, resp.
RN 74804-84-5
RN 2321-07-5

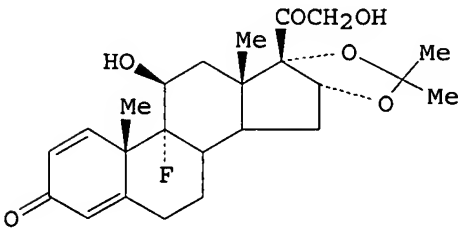
L18 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:172186 HCAPLUS
DOCUMENT NUMBER: 100:172186
ORIGINAL REFERENCE NO.: 100:26145a,26148a
TITLE: Tracer kinetic studies of glucose transport and metabolism using 18F-fluorosugars in isolated rat hearts
AUTHOR(S): Halama, James Rufus
CORPORATE SOURCE: Univ. Wisconsin, Madison, WI, USA
SOURCE: (1983) 169 pp. Avail.: Univ. Microfilms Int., Order No. DA8323053
From: Diss. Abstr. Int. B 1984, 44(9), 2639-40
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
RN 50-99-7

L18 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1983:417658 HCAPLUS
DOCUMENT NUMBER: 99:17658
ORIGINAL REFERENCE NO.: 99:2777a,2780a
TITLE: Effect of fluoroacetate on glucose synthesis in rat liver
AUTHOR(S): Bobyleva-Guarriero, V.; Dina, R.; Lauriola, P.; Masini, A.
CORPORATE SOURCE: Inst. Gen. Pathol., Univ. Modena, Modena, Italy
SOURCE: Fluoride (1983), 16(2), 117-28
CODEN: FLUOA4; ISSN: 0015-4725
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To get an insight into the increased glycemia in rats intoxicated with fluoroacetate (FAc) [144-49-0], the effect of this poison on the gluconeogenesis in isolated hepatocytes was studied. FAc (10 mM) inhibited the synthesis of glucose [50-99-7] from pyruvate [127-17-3] during the initial period of incubation, whereas the glucose synthesis from lactate [50-21-5] in the same period was unimpaired and sometimes activated. This activation could in part explain the increased glycemia is intoxicated animals. Thus, FAc acts at the level of the malate shuttle. In fact, the decrease of gluconeogenesis from pyruvate may be

due to the inhibition of this shuttle, with a consequent decrease of supply to the cytosol of NADH and Ca skeleton compds. The decrease in transport of NADH to cytosol could also explain the initial activation of gluconeogenesis from lactate. Under these conditions the optimal (lactate)/(pyruvate) ratio is reached earlier. In a more prolonged incubation period, the lack of malate shuttle function would lead to an inhibition of glucose synthesis from lactate also. Expts. were done with chicken hepatocytes, where there is no requirement for transport of oxaloacetate out of the mitochondria, which seems to confirm the proposed hypothesis.
RN 50-99-7
RN 144-49-0
RN 50-21-5
RN 127-17-3

L18 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:560180 HCAPLUS
DOCUMENT NUMBER: 97:160180
ORIGINAL REFERENCE NO.: 97:26681a,26684a
TITLE: Adipose hexose transport as examined by fluorescent glucose analogs
AUTHOR(S): DiPaola, Mario
CORPORATE SOURCE: New York Univ., New York, NY, USA
SOURCE: (1982) 206 pp. Avail.: Univ. Microfilms Int., Order No. DA8214798
From: Diss. Abstr. Int. B 1982, 43(2), 406-7
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L18 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:433644 HCAPLUS
DOCUMENT NUMBER: 97:33644
ORIGINAL REFERENCE NO.: 97:5667a,5670a
TITLE: Elevated concentrations of synthetic fluorinated glucocorticoid analogs transiently increase the intracellular exchangeable calcium in cultured bone cells
AUTHOR(S): Eilam, Y.; Silbermann, M.; Lewinson, D.; Szydel, N.; Toister, Z.; Harell, A.
CORPORATE SOURCE: Inst. Endocrinol., Ichilov Munic. Hosp., Tel Aviv/Jaffa, Israel
SOURCE: Calcified Tissue International (1982), 34(3), 258-64
CODEN: CTINDZ; ISSN: 0171-967X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB The influence of various glucocorticoids on the transport and accumulation of Ca2+ in cultured bone cells was investigated. For

measuring changes in the amount of intracellular exchangeable Ca2+, cultures were initially preincubated with 45Ca for 48 h thereby achieving a steady state. triamcinolone acetonide (I) [76-25-5] induced a transient increase in the cell content of exchangeable Ca2+, an effect that lasted for 5 h and was followed by a pronounced decrease noted at 24 h. A similar increase was observed with dexamethasone [50-02-2], whereas hydrocortisone [50-23-7] and corticosterone [50-22-6] were less effective. No changes took place with the use of deoxycorticosterone, progesterone, and estradiol. The effect of I on the cellular content of exchangeable Ca2+ was completely blocked by both cycloheximide and puromycin when added shortly after the addition of the corticosteroid to the culture system. To determine the effect of steroid hormones on the initial rate of Ca2+ influx into cultured cells, cultures were 1st preincubated with the various hormones and thereafter 45Ca was added. Only fluorinated glucocorticoid analogs such as I and dexamethasone increased the initial rate of Ca2+ influx. Ultrastructural examns. showed that in 5-day-old control cultures osteoblast-like cells show multiple aggregates of Ca pyroantimonate along their plasma membrane. In contrast, similar cells cultured in the presence of I for 3 h lacked such ppts. along their plasma membrane but instead contained aggregates of Ca pyroantimonate within enlarged mitochondria. Bone cells that were incubated with I for a longer period of time (24 h) exhibited hypertrophied mitochondria that were devoid of such ppts. Apparently, the potent synthetic analogs of glucocorticoids affect the rate of Ca influx into bone cells, the intracellular concentration of Ca, and the distribution of Ca within these cells.

RN 50-22-6
RN 50-23-7
RN 50-02-2
RN 76-25-5
RN 7440-70-2

L18 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1979:488618 HCAPLUS
DOCUMENT NUMBER: 91:88618
ORIGINAL REFERENCE NO.: 91:14315a,14318a
TITLE: Molecular probes for the mechanism of D-glucose transport across cellular membranes
AUTHOR(S): Taylor, N. F.; Gagneja, G. L.
CORPORATE SOURCE: Dep. Chem., Univ. Windsor, Windsor, ON, Can.
SOURCE: Cell Surf. Carbohydr. Chem., [Symp.] (1978), Meeting Date 1976, 269-90. Editor(s): Harmon, Robert E. Academic: New York, N. Y.
CODEN: 40YXA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Studied were the use of fluorodeoxymonosaccharides as probes for the stereospecific bonding of mediated glucose transport and the human erythrocyte, and of a model for the mode of inhibition of glucose transport by cytochalasin B in the human erythrocyte that is consistent with the binding requirements for the carrier protein in the membrane.
RN 14930-96-2
RN 50-99-7

L18 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1978:18868 HCAPLUS
DOCUMENT NUMBER: 88:18868
ORIGINAL REFERENCE NO.: 88:3015a,3018a
TITLE: Simulations of batch culture processes of Pseudomonas fluorescens
AUTHOR(S): Ootaguchi, Kazuhisa; Endo, Isao; Inoue, Ichiro
CORPORATE SOURCE: Tokyo Inst. Technol., Tokyo, Japan

SOURCE: Rikagaku Kenkyusho Hokoku (1977), 53(5), 179-84
CODEN: RKKHAO; ISSN: 0020-3084
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The glucose-oxidizing bacteria, P fluorescens, were cultivated batchwise at initial glucose concns. of 1.0, 2.5, 5.0, 7.5, and 10.0 mg/mL. The transport and metabolic processes of the bacteria were expressed by the relation between dimensionless sp. rates (Q) and dimensionless glucose concentration (G). The representative values of Q were the resp. maximum sp. rates observed at the logarithmic growth phase of the bacteria; that of G was the initial substrate concentration The batch cultivation system was represented in a block diagram and the state equation of the system was obtained on the basis of the above characteristics. Time dependences of glucose concentration in the medium, cell mass, sp. respiration rate, and sp. CO2 production rate were simulated by digital computer. The calculated results agreed well with exptl. data.
RN 50-99-7

L18 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1974:24633 HCAPLUS
DOCUMENT NUMBER: 80:24633
ORIGINAL REFERENCE NO.: 80:4059a,4062a
TITLE: Role of multivalent cations in the uptake and oxidation of glucose by Pseudomonas fluorescens
AUTHOR(S): Walker, Cynthia A.; Durham, Norman N.
CORPORATE SOURCE: Dep. Microbiol., Oklahoma State Univ., Stillwater, OK, USA
SOURCE: Biochemical Journal (1973), 136(2), 429-31
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Magnesium was the most effective single metal ion in the uptake and oxidation of glucose in induced and noninduced P. fluorescens. Mg2+ acted at the cell membrane, holding transport and respiratory proteins in the correct conformation for glucose accumulation by the cell. Ca2+, but not Mn2+ or Fe2+, could substitute for Mg2+.
RN 7439-95-4
RN 7440-70-2
RN 50-99-7

L18 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1967:400265 HCAPLUS
DOCUMENT NUMBER: 67:265
ORIGINAL REFERENCE NO.: 67:47a,50a
TITLE: Enzyic hydrolysis of the carbon-fluorine bond of α-D-glucosyl fluoride by rat intestinal mucosa. Localization of intestinal maltase
AUTHOR(S): Barnett, John E. G.; Jarvis, William T. S.; Munday, Kenneth A.
CORPORATE SOURCE: Univ. Southampton, Southmoton, UK
SOURCE: Biochemical Journal (1967), 10o, 699-704
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB α,D-Glucosyl fluoride was hydrolyzed by an extract of rat intestinal mucosa. The pH optimum was 6.6 and the Km was 0.4mM at 20°. Activity was assayed by release of either glucose or F-. The α-D-glucosyl fluoride hydrolase activity of the extract was associated with both mutarotase and α-D-glucosidase activities. Tris (5 mM) inhibited both the α-D-glucosidase and α-D-glucosyl fluoride hydrolase activities by 55% but did not inhibit mutarotase. The Ki of Tris for both enzyme activities was 2mM. The extract did not hydrolyze

melibiose and lactose. Mutarotase used both α-D-glucose and β-L-arabinose as substrates but the glucosyl fluoride hydrolase activity did not extend to β-L-arabinosyl fluoride. The thermal stability of α-D-glucosidase and α-D-glucosyl fluoride hydrolase was identical. Mutarotase was more thermolabile. A preparation of the brush border of intestinal epithelial cells contained both α-D-glucosyl fluoride hydrolase and α-D-glucosidase activities. In each precipitate and washing the ratio of the two activities was the same. All the mutarotase activity was in the 1st supernatant. Agidex, a fungal amyloglucosidase, cleaved glucosyl fluoride in addition to maltose. Tris inhibited both activities and in each case the Ki was 3mM. The probable identity of α-D-glucosyl fluoride hydrolase with α-D-glucosidase is discussed and a possible mechanism for the reaction suggested. Incubation of intestinal slices with α-D-glucosyl fluoride led to complete hydrolysis in 30 min. The glucose rapidly entered the cell and was metabolized, leaving the F- in the incubation medium. This result indicates that the intestinal α-D-glucosidase, although on the brush border, is located outside the site of active transport of sugars.

RN 9001-42-7
RN 9031-76-9
RN 2106-10-7